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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/818,143	03/26/2001	Michael G. Walker	PB-0004-1 CIP	2083

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EXAMINER	
CARLSON, KAREN C	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 03/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/818,143	WALKER ET AL.	
	Examiner	Art Unit	
	Karen Cochrane Carlson, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7, 10-19* is/are pending in the application.

4a) Of the above claim(s) *Claims 4-7, 10, 11, and 17-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 13-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

This Office Action is in response to the paper filed January 9, 2004. Claims 8, 9, and 12 have been canceled. Claims 4-7, 10, 11, and 17-19 are withdrawn from further examination by the Examiner because these claims are drawn to non-elected inventions. Claims 1-3 and 13-16, as drawn to SEQ ID NO: 6 or NO: 22, are under examination.

Priority remains set to the filing date of SN 09/169,289, filed October 9, 1998.

Withdrawal of Rejections

The rejection of the Claims under 35 U.S.C. 112, second paragraph, is withdrawn.

Maintenance of Rejections

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3 and 13-16 are again rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

The specification teaches that the polynucleotide of SEQ ID NO: 6, which encodes the polypeptide of SEQ ID NO: 22, is a matrix-remodeling gene because it is coexpressed with known matrix-remodeling genes. Coexpression of genes does not provide evidence regarding the function of the encoded gene product. Further, even if the gene encodes a protein involved in matrix-remodeling, its role or activity in matrix-remodeling has not been disclosed. For example, at page 1, line 11+, the specification teaches that matrix remodeling is associated with the construction, destruction, and reorganization of extracellular matrix components, and is essential in normal cellular functions and also in many disease processes including angiogenesis, arthritis, atherosclerosis, cancers, cardiomyopathy, diabetic necrosis, fibrosis, and ulceration. At page 23, the specification states that the known matrix remodeling gene products are categorized as

extracellular matrix component proteins, matrix proteases and matrix protease inhibitors, and regulatory proteins that control the expression of matrix remodeling genes. Pages 23-25 list the functions of 21 known matrix remodeling gene and their gene products. Taken in total, the assertion that SEQ ID NO: 6 and its encoded protein SEQ ID NO: 22 are involved in matrix remodeling because the gene is coexpressed with known matrix remodeling genes lacks basis for utility because coexpression of a gene does not correspond to gene or gene product function. The assertion that SEQ ID NO: 6 and its encoded protein SEQ ID NO: 22 is a matrix remodeling gene and gene product lacks basis for utility because the biological function of the gene product has not been taught.

Other utilities set forth in the specification for SEQ ID NO: 6 and its encoded protein SEQ ID NO: 22 include the diagnosis, prognosis, prevention, treatment, and evaluation of therapies for diseases associated with matrix remodeling such as cancer (including adenocarcinoma, leukemia, lymphoma, melanoma, myeloma, sarcoma, teratocarcinoma, and cancers of the adrenal gland, bladder, bone, bone marrow, brain, breast, cervix, gall bladder, ganglia, GI tract, heart, kidney, liver, lung, muscle, ovary, pancreas, parathyroid, penis, prostate, salivary glands, skin, spleen, testis, thymus, thyroid, uterus as set forth at page 15, line 21+), cardiomyopathy, arthritis, angiogenesis, diabetic necrosis, atherosclerosis, fibrosis, and ulceration (page 1, para. 2). As noted above, coexpression of genes says nothing about gene or gene product function. Additionally, the gene and gene product function has not been elucidated. Further, there is no showing that SEQ ID NO: 6 or its encoded protein SEQ ID NO: 22 is expressed in these tissues, these tissues greater than other tissues, or in cancerous versus non-cancerous tissue, for example.

The polynucleotide sequence consisting of SEQ ID NO: 6 may have utility because it encodes a protein having utility. At page 29, para. 1, SEQ ID NO: 22 is stated to be a 99 amino acid sequence that resembles RH1 and RH2 opsins, that are a family of G-protein coupled

receptors that mediate vision. Review of the art surrounding opsins shows that opsins are G-protein coupled receptor comprising approximately 350-400 amino acids, said receptor having seven transmembrane domains. See, for example, Cowman et al. (1986; Cell 44: 705-710), Kaushal et al. (1994; PNAS 91: 4024-4028), Pasqualetti et al. (2003; Eur. J. Neurosci. 18 : 364-372), and Zuker et al. (1985; Cell 40: 851-858). Thus, SEQ ID NO: 22 is not an opsin receptor, and SEQ ID NO: 6 does not encode an opsin receptor.

The asserted utilities are general utilities and do not form a substantial utility because further research is needed to identify or reasonably confirm a real world context of use for SEQ ID NO: 6 and its encoded protein SEQ ID NO: 22. Therefore, because Applicant has not disclosed any specific or substantial utility for the claimed invention, credibility will not be assessed.

Claims 1-3 and 13-16 are also again rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

At page 6, Applicants urge that the Examiner has mistaken that the Applicants assertion of utility for the claimed polynucleotides and polypeptide requires their having a specific role or activity in matrix remodeling. Rather, the claimed polynucleotides and polypeptide are co-expressed with matrix remodeling genes and that their "guilt by association" renders them as having a substantial likelihood that these genes are themselves involved in matrix remodeling but that this co-expression does not require that they function in any particular aspect of matrix remodeling. Thus, the Examiner's assertion that the claimed polynucleotides and polypeptide has activity in matrix remodeling is unfounded. In response, the most specific utility provided in the specification is that the polynucleotide having SEQ ID NO: 6 and polypeptide having SEQ ID

NO: 22 are matrix remodeling genes or encoded polypeptides. See page 6 wherein the specification states that:

> In particular, the method identifies polynucleotides, SEQ ID NOs: 1-20 and their encoded polypeptides, SEQ ID NOs: 21-23 (Figures 1-3) useful in diagnosis, prognosis, treatment, and evaluation of therapies for diseases associated with matlix-remodeling, particularly, angiogenesis, arthritis, atherosclerosis, cancers, cardiomyopathy, diabetic necrosis, fibrosis, and ulceration.

At pages 9-10:

> Using the method of the present invention, we have identified 20 novel polynucleotides that exhibit strong association, or coexpression, with known genes that are matrix-remodeling-specific. These known matrix-remodeling genes include BM-40, C/DSPG, collagen 1, H, H, and IV, CTGF, fibrillin, fibronectins, fibr-r, fibulin 1, HSPG, hevin, IGF 1, IGFBP, laminin, lumican, MGP, MMPS, TIMP 1, 2, and 3. The results presented in Tables 3 and 4 show that the expression of the 20 novel polynucleotides have direct or indirect association with the expression of known matrix-remodeling genes. *Therefore, the novel polynucleotide can potentially be used in diagnosis, prognosis, or treatment of diseases associated with matrix-remodeling, or in the evaluation of therapies for diseases associated with matrix-remodeling. Further, the proteins encoded by the 20 novel polynucleotides are potential therapeutic proteins or targets for identifying therapeutics against diseases associated with matrix-remodeling.*

Further, at page 7, Applicants urge that the claimed polynucleotides and polypeptide can be used as probes in gene and protein expression monitoring applications such as in drug development and toxicology testing. Applicants have provided declarations of Rockett, Iyer, and Bedilion and a host of references to support their view (which have not been provided on a PTO 1449).

Dr. Rockett discusses the importance of using polynucleotide and polypeptides expression profiling using a model of expression profile or a pattern of genes and protein expressed by treatment with known testicular toxins as standards, signatures, or fingerprints. Dr. Rockett's expertise and points are appreciated and well-taken. However, the specification does not establish any toxin which would induce the expression of SEQ ID NO: 6 or NO: 22 expression so that SEQ ID NO: 6 and NO: 22 can be a part of a pattern of expression in response to the toxin. Without this demonstration, the utility as a part of a pattern of gene expression induced by a toxin or like toxin is lost. It is not enough to say that SEQ ID NO: 6 or NO: 22 can be used in expression profiling; rather, in which toxin specific expression profile is SEQ ID NO: 6 or NO: 22 expressed?

Dr. Iyer discusses drug target validation and identity of secondary drug effects using expression profiling. Dr. Iyer's comments are well-taken. However, the specification does not establish any drug or pharmaceutical which would induce the expression of SEQ ID NO: 6 or NO: 22 expression so that SEQ ID NO: 6 and NO: 22 can be a part of a pattern of expression in response to the drug. Without this demonstration, the utility as a part of a pattern of gene expression induced by a drug is lost. It is not enough to say that SEQ ID NO: 6 or NO: 22 can be used in expression profiling; rather, in which drug specific expression profile is SEQ ID NO: 6 or NO: 22 expressed?

Dr Bedilion discusses the commercial need of customers to have more and more genes on each array. The customers use the array as a research tool, that is, they expose the array comprising many polynucleotides or polypeptides to toxins or drugs and detect the resulting expression pattern. However, the specification does not establish any toxin or drug which would induce the expression of SEQ ID NO: 6 or NO: 22 expression so that SEQ ID NO: 6 and NO: 22 can be a part of a pattern of expression in response to the toxin or drug. Without this demonstration, the utility as a part of a pattern of gene expression induced by a toxin or like toxin is lost. It is not

enough to say that SEQ ID NO: 6 or NO: 22 can be used in expression profiling; rather, in which toxin or drug specific expression profile is SEQ ID NO: 6 or NO: 22 expressed?

At page 9, Applicants duscuss the legal standard for 35 USC 101 and 112. While Applicants do not specifically argue the rejection, it appears that their point is that if a person of ordinary skill in the art would understand how to use the invention then it has utility. Again, in which toxin or drug specific expression profile is SEQ ID NO: 6 or NO: 22 expressed?

At pages 10-25, Applicants urge that SEQ ID NO: 6 and NO: 22 can be used in disease detection and diagnosis, and in toxicology testing. More information must be provided to establish this utility. For example, which disease is the expression of SEQ ID NO: 6 or NO: 22 associated with? How will they be used to detect or diagnose the disease? In response to which toxin with they be expressed?

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is 571-272-0946. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER